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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,607	10/23/2001	Lino Tavares	208.1004US	1029

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EXAMINER
GHALI, ISIS A D

ART UNIT	PAPER NUMBER
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/045,607	TAVARES ET AL.	
	Examiner	Art Unit	
	Isis A. Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/26/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-11,13,14,16,20,22-24,29,30,32-38 and 40-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11,13,14,16,20, 22-24,29,30,32-38 and 40-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' amendment filed 12/26/2006.

Claims 8-11, 13, 14, 16, 20, 22-24, 29, 20, 32-28, and 40-49 are included in the prosecution.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 8-11, 13, 14,16, 20-24, 29, 30, 32-38, and 40-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,910,205 ('205) combined with US 5,968,547 ('547).

The present claims 8-11, 13, 14,16 and 47 are directed to method of treating seasonal allergy or chronic urticaria comprising administering to the patient a transdermal delivery system containing loratadine, and the claims recite broad plasma levels and release rates as implied by the term "about". Claims 20-24, 29, 30, 32-38, 45 and 48 are directed to transdermal delivery system containing loratadine and provides broad plasma levels and release rates as implied by the term "about". Claims 46 and 49 are directed to method of treating seasonal allergy or chronic urticaria comprising administering to the patient a transdermal delivery system containing loratadine wherein the device comprises reservoir layer consisting essentially of 20-90% polymer, 0.1-30% softening agent, 0.1-20% loratadine and 0.1-30% solvent, and the claims recite broad plasma levels and release rates as implied by the term "about".

US '205 teaches a transdermal delivery system of loratadine for the treatment of allergic conditions (abstract). The system is formed of patch applied to skin for a specific period of time to permit the penetration of a desired amount of loratadine through the skin. The patch will be worn from one to four days and provides a total daily dose of 0.5 to 5 mg (col.2, lines 28-34). The patch comprises a reservoir having 10-20% loratadine; 50-60% solvent; and 20-35% fatty acid esters, i.e. softening agents (col.2, lines 19-29). The patch further comprises a backing layer and a release liner (col.2, line 64; col.3, line 6). The patch delivers 0.66 mg/15 cm^2/day of loratadine for the formulation comprising loratadine, solvent and skin softener (Table I). The reference disclosed that the dose may be varied depending on the size and age of the patient, and may also depends upon the severity of the condition being treated (col.3, lines 56-60). The frequency of

dosage application can be once every 3 days to once every 7 days (col.4, lines 5-10). The claimed delivery rates are met by the reference because the claimed rates are broadened by the term "about" and inclusive of the rates disclosed by the prior art. The prior art rate of delivery is 0.66 mg/15 cm^2/day, i.e. 44 $\mu g/cm^2$/day, and as claimed is about 16.2 $\mu g/cm^2$/day.

Additionally, the claimed release rates are determined by Valia-Chein cell and the prior art is silent regarding the test method and the art does not appear to rely on, or teach the test method. The Patent Office is not equipped with test facilities for result testing. Hence, the instantly claimed release rates are met by the prior art.

The reference does not teach the specific delivery profile of loratadine, the specific amounts of different ingredients, or specific structure and formulation of a transdermal device including polymer, solvents and softening agents in the transdermal delivery system.

US '547 teaches a transdermal drug delivery device for controlled delivery of drug for 3 days and maintaining the delivery for additional 2 days in accordance to the zero order kinetic of the drug (abstract). When the drug applied transdermally, it follows the pharmacokinetics to the provide its effect over prolonged period (col.4, lines 42-67, col. 5, lines 1-8). The device comprises backing layer, polymeric reservoir and protective liner (col.20, lines 17-27). The reservoir comprising: 1-90% of polymeric material, 0.1-30% of the drug, 0.1-30% softener, and 0.1-30% of solvent (col.20, lines 55-60). The polymeric material of the reservoir is pressure sensitive adhesive and contains rubber, silicone or block-copolymers (col.18, lines 55-65). The solvents used

include those contain at least one acidic group, particularly, monoesters of dicarboxylic acids, such as monomethyl glutarate and monomethyl adipate (col.20, lines 5-10). The softeners include medium chain triglycerides of the caprylic/capric acids or coconut oil, undecanol, octanol, and dodecanol (col.19, lines 58-68). The backing is laminate of polymer and aluminum foil (col.18, lines 25-30).

It is evident from the disclosure of US '547 that when the drug is included in the described transdermal device, the drug follows and is delivered according to its pharmacokinetics for period of 5 days as desired by applicants. The structure and formulation of the reservoir of the present transdermal device are identical to that of US '547. Applicants disclosed on the paragraph bridging page 23 and 24 that the pharmacokinetic information for oral loratadine is available in the literature and a release rate for a loratadine transdermal delivery system was calculated from the available data. Applicants also admit on page 24, first full paragraph that any type of transdermal delivery system may be used in accordance with the methods of the present invention so long as the desired pharmacokinetic are attained over at least 3 days to about 8 days.

Therefore, having available within hands the disclosure of US '205 that teaches loratadine delivered transdermally and US '547 that teaches drug delivery rate over 3-5 days following the pharmacokinetics of the drug and is attained by specific structure and formulation of a transdermal drug delivery system, along with the pharmacokinetics of loratadine, one having ordinary skill in the art at the time of the invention would have designed transdermal drug delivery device to deliver loratadine as disclosed by US '205

and use the device disclosed by US '547 and would calculate the transdermal release rates from the available pharmacokinetic data of loratadine to achieve a transdermal delivery device having the structure and reservoir formulation comprising polymer, softener, solvent and loratadine that delivers loratadine at a delivery rate in accordance to its pharmacokinetics to treat patients suffering from allergic reactions with great success.

The determination of the relative release rate via an in-vitro permeation test utilizing a Valia-Chien cell is known in the art and it is not part of the claimed method of treating allergic rhinitis; or even a part of the transdermal device that provide particular plasma levels of loratadine. It is only an in-vitro diagnostic test that is expected to provide the same results obtained from two similar delivery devices tested under the same circumstances, and the recitation of this in-vitro test does not impart patentability to claims directed to method of treating allergic rhinitis or claims directed to transdermal device applied to patients to provide specific plasma levels of loratadine, i.e. in vivo use.

Response to Arguments

4. Applicant's arguments filed 12/26/2006 have been fully considered but they are not persuasive. Applicants traverse this rejection by arguing that:

- Applicants argue that the presently claimed invention is not obvious over the Kogan patent in view of the Reder patent because Kogan patent does not teach a transdermal delivery device including polymer, solvents and softening and one skilled in the art would not be motivated to combine the Reder patent with the Kogan patent as each reference is directed to different utilities because Kogan patent is limited to transdermal delivery devices of loratadine and Reder patent is

limited to transdermal delivery devices of buprenorphine. Reder patent is specifically directed to buprenorphine and does not teach or suggest that the transdermal formulations and methods described therein are suitable for use with any agent other than buprenorphine.

In response to this argument, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, having available within hands the disclosure of US '205 that teaches loratadine delivered transdermally and US '547 that teaches drug delivery rate over 3-5 days following the pharmacokinetics of the drug that is attained by specific structure and formulation of a transdermal drug delivery system, along with the pharmacokinetics of loratadine, one having ordinary skill in the art at the time of the invention would have designed transdermal drug delivery device to deliver loratadine as disclosed by US '205 and use the device disclosed by US '547 and would calculate the transdermal release rates from the available pharmacokinetic data of loratadine to achieve a transdermal delivery device having the structure and reservoir formulation comprising polymer, softener, solvent and loratadine that delivers loratadine at a delivery rate in accordance to its pharmacokinetics to treat patients suffering from allergic reactions with great success. It has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem

with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the cited prior art in the field of applicant's endeavor and Kogan is concerned about transdermal delivery of loratadine and Reder is concerned about transdermal delivery of a drug over 3-5 days following the pharmacokinetics of the drug that is attained by specific structure and formulation of a transdermal drug delivery system, and their combination is reasonable as stated above.

- Applicants argue that even if the Kogan patent and the Reder patent were combined, one skilled in the art would not arrive at the presently claimed invention because independent claims 8, 20 and 46 all recite that the active agent is solely limited to loratadine and the formulations and methods of the Reder patent all contain buprenorphine as a necessary ingredient. Therefore, looking as the Reder reference as a whole, it is impermissible for the Examiner to "pick and choose" specific ingredients from the Reder patent to combine with the Kogan patent, without considering the entire teachings of the reference.

In response to this argument, it is established that in considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different

problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972). Kogan teaches loratadine administered transdermally and it is evident from the disclosure of US '547 that when the drug is included in the described transdermal device, the drug follows and is delivered according to its pharmacokinetics for period of 5 days as desired by applicants. The structure and formulation of the reservoir of the present transdermal device are identical to that of US '547. Applicants disclosed on the paragraph bridging page 23 and 24 that the pharmacokinetic information for oral loratadine is available in the literature and a release rate for a loratadine transdermal delivery system was calculated from the available data. Applicants also admit on page 24, first full paragraph that any type of transdermal delivery system may be used in accordance with the methods of the present invention so long as the desired pharmacokinetic are attained over at least 3 days to about 8 days.

- Applicants further submit that the neither Kogan nor Reder teach or suggest the specific delivery profiles of loratadine as claimed in independent claims 8, 20 and 46. Therefore, a combination of the references cannot obviate independent claims 8, 20, and 46 of the present invention and one skilled in the art would not consider that the term "about" broadens the recited rate of 16.2 μg/cm2/hr to 44 μg/cm2/day, which is about 270% than the recited value.

In response to this argument, and upon careful review to Kogan reference, it is noticed that flux rate ranges from 6 $\mu g/cm^2/day$ to 58 $\mu g/cm^2/day$ that the release rate disclosed by Kogan obviates the claimed delivery rates because the delivery rate

disclosed by Kogan is 44 μg/cm^2/day and the claimed delivery rate has lower range from 2 to 16.2 μg/cm^2/hr which is equivalent to 48 to 389 μg/cm^2/day. Therefore, the claimed delivery rates are met by the reference because the claimed rates overlapped with the rates disclosed by the reference.

- Applicants argue that the Examiner's rejection is based on the impermissible hindsight reasoning afforded by the present invention.

In response to this applicant's, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

- Applicants argue that Kogan patent states that a surprising result was provided by a loratadine transdermal device which contains a combination of a volatile solvent, an essential oil and a fatty acid ester, and the present claim 46 contains the language "consisting essentially of". Further, the combination of Kogan patent and the Reder patent would necessarily result in a transdermal delivery device which contains an essential oil as one skilled in the art would lack motivation to formulate a device that does not include an essential oil.

In response to this argument, it is established that the expression "consisting essentially of" limits the scope of the claim to the specified ingredients, and those that do not materially affect the basic and novel characteristics of the composition. *In re Janakirama-Rao*, 317 F 2d 951, 137 USPQ 893 (CCPA 1963). When applicant

contends that modifying components in the reference's composition are excluded by the recitation of "consisting essentially of", applicant has the burden of showing the basic and novel characteristics of the claimed composition, i.e. showing that the introduction of these components would materially change the characteristics of applicant's composition. *In re De Lajarte,* 337 F 2d 870, 143 USPQ 256 (CCPA 1964). The present invention desired to include skin softener and solvents, and the essential oil disclosed by Kogan reads on solvent and skin softened.

- Applicants argue that the functional limitation regarding "Valia-Chien test" must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. Applicants argue that the specific release rates recited in the present claims should be evaluated and considered, just like any other limitation of the claim in determining patentability of the present claims.

In response to this argument, it is noted that the determination of the relative release rate via an in-vitro permeation test utilizing a Valia-Chien cell is known in the art and it is not part of the claimed method of treating allergic rhinitis; or even a part of the transdermal device that provide particular plasma levels of loratadine. It is only an in-vitro diagnostic test that is expected to provide the same results obtained from two similar delivery devices tested under the same circumstances, and the recitation of this in-vitro test does not impart patentability to claims directed to method of treating allergic rhinitis or claims directed to transdermal device applied to patients to provide specific plasma levels of loratadine, i.e. in vivo use. Additionally, the claimed release rates are determined by Valia-Chein cell and the prior art is silent regarding the test method and

the art does not appear to rely on, or teach the test method. The Patent Office is not equipped with test facilities for result testing. Hence, the instantly claimed release rates are met by the prior art.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone

number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis A Ghali
Primary Examiner
Art Unit 1615

ISIS GHALI
PRIMARY EXAMINER